Bone Mineral Density Studies

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Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for bone density studies when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
An initial measurement of BMD at the hip or spine may be considered medically necessary to assess fracture risk and the need for pharmacologic therapy in both women and men who are considered at risk for osteoporosis. BMD testing may be indicated under the following conditions:

- Women age 65 and older, regardless of other risk factors;
- Men age 70 and older, regardless of other risk factors;
- Younger postmenopausal women about whom there is a concern based on their risk factors;
- Men age 50-70 about whom there is a concern based on their risk factors;
- Adults with a condition or taking a medication associated with low bone mass or bone loss.

Repeat measurement of central (hip/spine) BMD for individuals who previously tested normal (does not require pharmacologic treatment) may be considered medically necessary at an interval not more frequent than every 3–5 years; the interval depends on patient risk factors.

Regular (not more frequent than every 2-3 years) serial measurements of central BMD to monitor treatment response may be considered medically necessary when the information will affect treatment decisions such as duration of therapy.

Peripheral BMD testing may be considered medically necessary when conventional central (hip/spine) DXA screening is not feasible or in the management of hyperparathyroidism, where peripheral DXA at the forearm (ie, radius) is essential for evaluation.
When Policy Topic is not covered

BMD measurement using ultrasound densitometry, quantitative computed tomography, or dual x-ray absorptiometry of peripheral sites is considered **investigational except as noted above**.

A bone density study is considered **screening** for those individuals not considered at high risk for osteoporosis.

Initial or repeat BMD measurement is not indicated unless the results will influence treatment decisions.

Considerations

The decision to perform bone density assessment should be based on an individual’s fracture risk profile and skeletal health assessment. (1) In addition to age, gender, and bone mineral density (BMD), risk factors included in the World Health Organization (WHO) Fracture Risk Assessment Model (FRAX) are:

- Low body mass index;
- Parental history of hip fracture;
- Previous fragility fracture in adult life (i.e., occurring spontaneously, or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture);
- Current smoking or alcohol 3 or more units/day, where a unit is equivalent to a standard glass of beer (285ml), a single measure of spirits (30ml), a medium-sized glass of wine (120ml), or 1 measure of an aperitif (60ml);
- A disorder strongly associated with osteoporosis. These include rheumatoid arthritis, osteopenia, type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition or malabsorption, and chronic liver disease;
- Current exposure to oral glucocorticoids or the patient has been exposed to oral glucocorticoids for more than 3 months at a dose of prednisolone of 5mg daily or more (or equivalent doses of other glucocorticoids).

A 2011 joint position statement from the International Society for Clinical Densitometry (ISCD) and the International Osteoporosis Foundation (IOF) includes the official position that FRAX with BMD predicts risk of fracture better than clinical risk factors or BMD alone. (2) In addition, the joint position statement states that measurements other than BMD or T score at the femoral neck by DXA are not recommended for use with FRAX.

The FRAX model does not include a recommendation about which patients to further assess or treat. The FRAX website (1) states that this is a matter of clinical judgment and recommendations may vary by country.
Bone Mineral Density Technologies
Ultrasound densitometry is an office-based technology. As discussed further in the Rationale section, it is unknown whether this technology can be used to predict response to pharmacologic therapy (i.e., reduce fractures).

Dual x-ray absorptiometry (DXA) of central sites (i.e., hip and spine) is the most commonly used technique, but peripheral DXA and quantitative CT scanning are sometimes used, based on local availability. Peripheral measurement can identify patients with low bone mass, but does not predict response to pharmacologic therapy is not a substitute for central DXA measurements. Therefore, central DXA is required for both the initial diagnosis and repeat BMD assessments.

Peripheral scans performed concurrently with axial scans are considered mutually exclusive and are not eligible for separate reimbursement. The peripheral scan will disallow as a component of the axial scan.

Peripheral measurement of BMD may be appropriate:
- If the hip/spine or hip/hip cannot be done or the patient is over the table limit for weight;
- Hyperparathyroidism, where the forearm is essential for diagnosis

In pediatric patients, total body calcium is preferred because it helps reduce the issue of following patients with growing bones.

### Description of Procedure or Service

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Bone density studies can be used to identify individuals with osteoporosis and monitor response to osteoporosis treatment, with the goal of reducing the risk of fracture. Bone density is most commonly evaluated with dual x-ray absorptiometry (DXA); other technologies are also available.
For individuals who are eligible for screening of BMD based on risk factor assessment who receive DXA analysis of central sites (hip or spine), the evidence includes large cohort studies, observational studies, and systematic reviews. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, health status measures, quality of life, hospitalizations, medication use, and resource utilization. BMD measurements with central DXA identify individuals at increased risk of fracture. There is sufficient evidence that osteoporosis medications are effective at reducing fracture risk in postmenopausal women with BMD in the osteoporotic range identified by central DXA. Therefore, a chain of evidence establishes that screening BMD with central DXA is likely to improve health outcomes. Evidence to support serial or repeat measurement of BMD is less compelling; nonetheless, the available evidence and the consensus of clinical evidence-based guidelines support at least a 2-year interval in BMD measurement to monitor response to pharmacologic therapy. Finally, available evidence suggests that at least a 3- to 5-year timeframe is reasonable for repeat measurement of BMD in individuals who initially tested normal and to monitor pharmacologic therapy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are eligible for screening of BMD based on risk factor assessment who receive ultrasound densitometry, or quantitative computed tomography, or DXA analysis of peripheral sites, the evidence includes observational studies and systematic reviews. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, health status measures, quality of life, hospitalizations, medication use, and resource utilization. These technologies are not commonly used for BMD measurements in practice and no studies have shown that they can select patients who benefit from treatment for osteoporosis. There is little to no evidence on the usefulness of repeat measurement of BMD using these techniques. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Background**

**Bone Mineral Density**

Risk factors for fracture include low bone mass, low bone strength, a personal history of fracture as an adult, or a history of fracture in a first-degree relative. Osteoporosis, defined as low bone mass leading to an increased risk of fragility fractures, is an extremely common disease in the elderly population due to age-related bone loss in both sexes and menopause-related bone loss in women. The World Health Organization (WHO) has diagnostic thresholds for osteoporosis based on bone mineral density (BMD) measurements compared with a T score, which is the standard deviation difference between an individual’s BMD and that of a young-adult reference population. Conditions that can cause or contribute to osteoporosis include lifestyle factors such as low intake of calcium, high intake of alcohol or cigarette smoking, and thinness. Other risk factors for osteoporosis include certain endocrine, hematologic, gastrointestinal tract and genetic disorders, hypogonadal states, and medications.
BMD can be measured using different techniques in a variety of central (ie, hip or spine) or peripheral (ie, wrist, finger, heel) sites. While BMD measurements are predictive of fragility fractures at all sites, central measurements of the hip and spine are the most predictive. Fractures of the hip and spine (ie, vertebral fractures) are also considered to be the most clinically relevant. BMD is typically expressed as a T score.

The utility of screening BMD measurements can be established by demonstrating that screening identifies a population at increased risk of fracture and that, by treating those at-risk individuals, the rate of fractures is reduced thereby lowering fracture-related morbidity and mortality. These potential benefits of screening should outweigh the risks of screening (radiation exposure) or false positives (initiation of unnecessary treatment).

**Osteoporosis Treatment**

Treatment of osteoporosis includes both lifestyle measures (eg, increased intake of calcium and vitamin D, exercise, smoking cessation) and pharmacologic measures. Current pharmacologic options include bisphosphonates such as alendronate (ie, Fosamax), selective estrogen receptor modulators such as raloxifene (ie, Evista), the recombinant human parathyroid hormone teriparatide (ie, Forteo), and calcitonin. An updated 2014 systematic review funded by the Agency for Healthcare Research and Quality found good-quality evidence that bisphosphonates, denosumab, teriparatide, and raloxifene reduce fracture risk in postmenopausal women with BMD in the osteoporotic range and/or preexisting hip or vertebral fracture.¹

The decision to perform bone density assessment should be based on an individual’s fracture risk profile and skeletal health assessment. In addition to age, sex, and BMD, risk factors included in the WHO Fracture Risk Assessment (FRAX) Tool² are:

- Low body mass index;
- Parental history of hip fracture;
- Previous fragility fracture in adult life (ie, occurring spontaneously or a fracture arising from trauma, which, in a healthy individual, would not have resulted in a fracture);
- Current smoking or 3 or more units of alcohol daily, where a unit is equivalent to a standard glass of beer (285 mL), a single measure of spirits (30 mL), a medium-sized glass of wine (120 mL), or 1 measure of an aperitif (60 mL);
- A disorder strongly associated with osteoporosis, which includes rheumatoid arthritis, type I (insulin-dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition or malabsorption, and chronic liver disease;
- Current exposure to oral glucocorticoids or exposure to oral glucocorticoids for more than 3 months at a dose of prednisolone 5 mg daily or more (or equivalent doses of other glucocorticoids).
A 2011 joint position statement from the International Society for Clinical Densitometry and the International Osteoporosis Foundation included the official position that FRAX with BMD predicts risk of fracture better than clinical risk factors or BMD alone. In addition, the joint position statement indicated that measurements other than BMD or T score at the femoral neck by DXA are not recommended for use with FRAX.3 The FRAX tool does not include a recommendation about which patients to further assess or treat. The FRAX website states that this is a matter of clinical judgment and recommendations may vary by country.2

**Measurement Tools**
The following technologies are most commonly used to measure BMD.

**Dual X-Ray Absorptiometry**
Dual x-ray absorptiometry (DXA) is probably the most commonly used technique to measure BMD because of its ease of use, low radiation exposure, and its ability to measure BMD at both the hip and spine. DXA can also be used to measure peripheral sites, such as the wrist and finger. DXA generates 2 x-ray beams of different energy levels to scan the region of interest and measures the difference in attenuation as the low- and high-energy beams pass through the bone and soft tissue. The low-energy beam is preferentially attenuated by bone, while the high-energy beam is attenuated by both bone and soft tissue. This difference in attenuation between the 2 beams allows for correction for the irregular masses of soft tissue, which surround the spine and hip, and therefore the measurement of bone density at those sites.

**Quantitative Computed Tomography**
Quantitative computed tomography (QCT) depends on the differential absorption of ionizing radiation by calcified tissue and is used for central measurements only. Compared with DXA, QCT is less readily available and associated with relatively high radiation exposure and relatively high cost.

**Ultrasound Densitometry**
Ultrasound densitometry is a technique for measuring BMD at peripheral sites, typically the heel but also the tibia and phalanges. Compared with osteoporotic bone, normal bone demonstrates higher attenuation of the ultrasound wave and is associated with a greater velocity of the wave passing through bone. Ultrasound densitometry has no radiation exposure, and machines may be purchased for use in an office setting.

These techniques dominate BMD testing. Single- and dual-photon absorptiometry and radiographic absorptiometry are now rarely used and may be considered obsolete.

Note: Vertebral fracture assessment with DXA in addressed elsewhere.
Regulatory Status
Several devices that measure bone density have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Some examples include:

- QCT-Bone Mineral Phantom (Image Analysis) in 1985
- Quantitative Digital Radiography (QDR™; Hologic) x-ray bone densitometer using dual x-ray absorptiometry in 1987
- Lunar DPX bone densitometer (now GE Lunar DPX NT®; GE Healthcare) in 1988
- Accudxa2® Bone Mineral Density Assessment System (Lone Oak Medical Technologies, Doylestown, PA) in 2012.

In addition, some ultrasound bone sonometers have been approved by FDA through the premarket approval (PMA) process. One example is the Sahara® Clinical Bone Sonometer (Hologic), which received approval in March 1998. Its intended use is for quantitative ultrasound measurement of the calcaneus (heel bone), the results of which can be used in conjunction with other clinical risk factors as an aid in the diagnosis of osteoporosis and medical conditions leading to reduced bone density, and ultimately in the determination of fracture risk.

Rationale
This evidence review was originally created in December 1995 and has been updated regularly with searches of the MEDLINE database. The most recent literature review was performed through January 25, 2017. Following is a summary of key literature to date.

Initial Measurement of Bone Mineral Density
Early versions of this evidence review were based in part on 1998 guidelines from the National Osteoporosis Foundation (NOF) and 2 TEC Assessments (1999, 2002). Because no data were available from randomized screening trials, the TEC Assessments focused on the evaluating the utility of bone mineral density (BMD) measurement in selecting patients for pharmacologic treatment to reduce risk of fracture. The TEC Assessments concluded that while both dual x-ray absorptiometry (DXA) and ultrasound densitometry were equivalent in predicting fracture risk, the 2 techniques appeared to identify different populations of at-risk patients. In addition, calcaneal ultrasound densitometry did not meet TEC criteria as a technique to predict response to pharmacologic therapy.

A 2005 meta-analysis of data from 9891 men and 29,082 women (from 12 cohort studies in Europe and Canada) found that BMD measurement at the femoral neck with DXA was a strong predictor of hip fractures for both sexes. At age 65 years, the relative risk for osteoporotic fractures increased by 1.4 (95% confidence interval [CI], 1.3 to 1.5) in men and by 1.4 (95% CI, 1.3 to 1.5) in women for each standard deviation decrease in BMD. Data for measurement of BMD using ultrasound and peripheral DXA were available from 3 cohorts. The predictive
ability of these devices was less than that of DXA measurements at the femoral neck.

A systematic review of the evidence to update U.S. Preventive Services Task Force (USPSTF) recommendations on screening for osteoporosis was published in 2010. USPSTF reviewers stated that most DXA testing includes central DXA (ie, measurements at the hip and lumbar spine) and that most randomized controlled trials (RCTs) of osteoporosis medications have had study inclusion criteria based on the findings of central DXA. Reviewers found that calcaneal quantitative ultrasound (QUS) measurement could also predict fracture but has a low correlation with DXA. Consequently, the clinical relevance of calcaneal QUS findings is unclear because medication studies have not selected patients based on QUS findings. In addition, the investigators reviewed large population-based cohorts on DXA screening and concluded that the predictive performance of DXA is similar for women and men.

In 2013, Gadam et al performed a cross-sectional analysis of data to assess the incremental predictive ability of BMD measured using DXA when added to the Fracture Risk Assessment (FRAX) Tool model. The study included 151 subjects (145 women, 6 men) older than 50 years of age without a prior osteoporosis diagnosis and who were not being treated with U.S. Food and Drug Administration (FDA)–approved medications for osteoporosis. Of the 151 subjects, predictions of 10-year fracture risk were identical for 127 (84%) patients when BMD was added to the FRAX model compared with the FRAX model without BMD. Of the subjects who had different risk estimates, the difference in risk prediction resulted in an additional 2 patients meeting the NOF threshold for treatment when BMD was added to the FRAX model. Age was the only risk factor that differed significantly between participants with identical versus different recommendations (p<0.001). Subjects who were younger (mean age, 64 years) were more likely to receive identical predictions than older subjects (mean age, 76 years). The study had a relatively small sample size and lacked longitudinal data on fractures. It provides some initial evidence that BMD may not add substantially to the predictive ability of the FRAX models, but these findings need to be corroborated in prospective studies with larger sample sizes.

Crandall et al (2015) reported results from 11,392 participants in the Women’s Health Initiative (WHI) BMD Cohort, a prospective observational study of postmenopausal women with a mean follow-up of 8.5 years. Each standard deviation decline in lower BMD measured with central DXA was associated with higher wrist fracture risk, the adjusted hazard ratio (HR) being 1.7 (95% CI, 1.4 to 1.9) for femoral neck BMD and 1.5 (95% CI, 1.3 to 1.6) for lumbar spine BMD.

Cauley et al (2016) reported risk factors for hip fractures in 5994 men with a mean of 8.6 years of follow-up from the Osteoporotic Fractures in Men Study. Femoral neck BMD was measured using DXA. The incidence rate of hip fracture 33.4 per 1000 person-years in men with BMD T scores less than -2.5 who also had 4 or more risk factors, 14.5 per 1000 person-years in men age 80 years and older with 3 or more major comorbidities, and 0.88 per 1000 person-years in men age
less than 70 years with zero comorbidities. Low BMD by World Health Organization classification (T score < -2.5 ) was highly associated with hip fracture (hazard ratio [HR], 3.3; 95% CI, 2.7 to 3.9) in a competing risk model after adjusting for several other fracture risk factors (eg, age, previous fracture).

**Section Summary: Initial Measurement of Bone Mineral Density**
Central DXA is the most widely used method for measuring BMD. Several large studies have demonstrated a relation between fracture risk and BMD as measured by DXA in women and men. Most RCTs of the osteoporosis medications have had study inclusion criteria based on central DXA. These RCTs have shown that several osteoporosis medications are effective at reducing fracture risk in postmenopausal women with BMD in the osteoporotic range identified by central DXA and/or preexisting hip or vertebral fracture. This chain of evidence establishes that measuring BMD with central DXA improves health outcomes. There is less evidence for other methods of measuring BMD. BMD measured with other techniques may also be associated with fracture risk but has not been used to select participants for trials of osteoporosis medications.

**Repeat Measurement of BMD for Individuals Without Osteoporosis on Initial Screen**
In the analysis from the WHI BMD cohort (2015) previously described, changes in central DXA were examined over a 3-year period. A total of 9172 women had baseline and year 3 measures of femoral neck BMD and 9216 women had baseline and year 3 measures of lumbar spine. Decrease in femoral neck BMD between baseline and year 3 was associated with increased risk of subsequent wrist fracture (HR=1.2; 95% CI, 1.0 to 1.3; p=0.03). Change in lumbar spine BMD was not associated with wrist fracture by year 3 (HR=1.1; 95% CI, 0.95 to 1.2; p=0.22).

Leslie et al (2016) reported on repeat BMD measurements in clinical practice for fracture risk assessment from a large clinical BMD database for Manitoba, Canada, of women and men ages 50 years and older from 1990 to 2009. BMD was measured in the hip, lumbar spine, and femoral neck using DXA. A total of 50,215 participants had 1 BMD measurement, 14,619 had a second measurement, 4722 had a third measurement, and 1500 had a fourth measurement. The mean time between measurements was 4.2 years. Total hip BMD was predictive of major osteoporotic fracture at each time point. The association between BMD and major osteoporotic fracture was similar for the first and second BMD measurements: adjusted hazard ratios per standard deviation were 1.5 (95% CI, 1.3 to 1.6) and 1.6 (95% CI, 1.5 to 1.8), respectively. The hazard ratio for the second measurement was similar when stratified by preceding change in BMD or osteoporosis therapy.

A 2013 study by Berry et al did not find that changes in BMD 4 years after initial measurement added substantially to the prediction of fracture risk in untreated subjects. The authors included 210 women and 492 men (mean age, 75 years) from the Framingham Osteoporosis Study, a population-based cohort study, who had 2 BMD measurements (mean, 3.7 years apart) and did not have a hip fracture
before the second test. BMD of the femoral neck was measured using a dual-photon absorptiometer from 1987 through 1991 and DXA from 1992 through 1999. Median follow-up was 9.6 years after the second BMD test. During this time, 76 individuals experienced a hip fracture and 113 had a major osteoporotic fracture (fracture of the hip, spine, forearm, or shoulder). In receiver operating curve analyses, adding repeat BMD to a model containing baseline BMD did not meaningfully improve the model’s ability to predict hip fracture (area under the curve [AUC], 0.72; 95% CI, 0.66 to 0.79). When percent change in BMD was used, the AUC was 0.71 (95% CI, 0.65 to 0.78) in a model including only baseline BMD and 0.68 (95% CI, 0.62 to 0.75) in a model including percent change in BMD.

A 2012 multicenter prospective study by Gourlay et al have provided data on the optimal bone density screening interval in a large cohort of women with normal BMD measured by DXA or osteopenia at an initial screen. The investigators included 4957 women ages 67 years or older who had BMD data at 2 or more examinations or at 1 examination before a competing risk event (hip or clinical vertebral fracture). The study only included women who were candidates for osteoporosis screening. Other individuals, such as those with osteoporosis at baseline or with a history of a hip or clinical vertebral fracture, were excluded, because they would already be candidates for pharmacologic treatment. The primary study outcome was the estimated time interval for 10% of participants to make the transition from normal BMD or osteopenia at baseline to osteoporosis before a hip or clinical vertebral fracture occurred and before starting osteoporosis treatment. For women with normal BMD at baseline, the estimated BMD testing interval was 16.8 years (95% CI, 11.5 to 24.6 years). The study found that the estimated BMD testing interval was 17.3 years (95% CI, 13.9 to 21.5 years) for women with mild osteopenia at baseline, 4.7 years (95% CI, 4.2 to 5.2 years) with moderate osteopenia, and 1.1 years (95% CI, 1.0 to 1.3 years) for women with advanced osteopenia.

Longitudinal changes in BMD measured by central DXA, as a function of age and antiresorptive agents, were reported in 2008 by the Canadian Multicentre Osteoporosis Study Research Group. Among a random selection of 9423 men and women from 9 major Canadian cities, 4433 women and 1935 men (cumulatively 70%) were included for analysis. The subjects were 25 years of age or older with BMD measurements repeated 3 or 5 years apart; they tended to have better health than the 30% who did not have longitudinal data and who were excluded from analysis. Results showed that annual rates of bone loss, measured at the hip or femoral neck, increased between 25 and 85 years of age in women who were not on antiresorptive therapy, with accelerated periods of bone loss around menopausal transition (age range, 40-54 years) and after 70 years of age. Antiresorptive therapy, which primarily consisted of hormone replacement when the study began in 1995, was associated with attenuated bone loss across all age ranges. For women 50 to 79 years of age, the average loss in BMD over a 5-year period was 3.2% in nonusers of antiresorptive therapy and 0.2% in women who used antiresorptive therapy. The pattern in men was generally similar to that of women with 2 exceptions: BMD loss began earlier in men and the rate of change
remained relatively constant between 40 and 70 years of age. Notably, BMD at the lumbar spine did not parallel measurements at the hip and femoral neck, suggesting that vertebral bone density assessment may be obscured by degenerative changes in the spine or other artifact. The report concluded that “although current guidelines recommend that measurements of bone density be repeated once every 2 to 3 years, our data suggest that, at this rate of testing, the average person would exhibit change well below the margin of error, especially since only 25% of women experienced a loss of bone density that exceeded 5% over 5 years.”

In 2009, Frost et al published a prognostic model to determine the optimal screening interval for a subject without osteoporosis (defined as T score > -2.5). They used prospective population-based data collected from 1008 women and 750 men who were nonosteoporotic at baseline; participants received BMD screening every 2 years and had a median follow-up of 7.1 years. The prognostic model included 2 variables: age and initial BMD score. Results were stratified for these variable, presented tabularly, showing estimated time to reach 20% risk of sustaining a fracture or osteoporosis. Most of the time estimates were 3 years or longer. The estimated shortest time to reach a 20% risk was 2.4 years; this was for women 80 years and older with a baseline T score of -2.2. For a typical screening candidate (a 65-year-old woman with a baseline T score of -1.0), the estimated time to reach a 10% risk of fracture was 3.8 years and to reach a 20% risk of fracture was 6.5 years. Overall, the study suggested that the 3- to 5-year time interval for repeat measurement of BMD in people who tested normal is reasonable but that an individualized model could result in longer or shorter recommended retesting intervals.

A 2007 study by Hillier et al did not find that follow-up central DXA BMD measurements 8 years after a baseline screen provided substantial value in terms of predicting risk of fracture. The study included 4124 women ages 65 years and older and assessed total hip BMD at initial and follow-up screening examinations. In analyses adjusted for age and weight change, the initial and repeat BMD measurements had similar associations with fracture risk; this included risk of vertebral fractures, non-vertebral fractures, and hip fractures. Stratifying the analysis by initial BMD T scores (ie, normal, osteopenic, osteoporotic) did not alter findings.

Section Summary: Repeat Measurement of BMD for Individuals Without Osteoporosis on Initial Screen
Scant research has been done on the frequency of BMD monitoring for osteoporosis. The available research has evaluated repeat measurement with central DXA. Evidence on whether repeat measurements add to risk prediction compared with a single measurement is mixed. A longitudinal study suggests that a 3- to 5-year interval for repeat measurement of BMD in people who tested normal at baseline is reasonable, although the optimal interval may differ depending on risk factors.
Serial Measurement of Central BMD to Monitor Response to Bisphosphonate Treatment

In 2009, Bell et al. conducted a secondary analysis of data from the Fracture Intervention Trial (FIT), which randomized 6459 postmenopausal women with low BMD to treatment with bisphosphonates or to placebo; women underwent annual bone density scans. The investigators estimated between-person (treatment-related) variation and within-person (measurement-related) variation in hip and spine BMD measured by central DXA over time to assess the value of repeat BMD scans for monitoring response to treatment. After 3 years, the mean cumulative increase in hip BMD was 0.30 g/cm² in the alendronate group compared with a mean decrease of 0.012 g/cm² in the placebo group. Moreover, 97.5% of patients treated with alendronate had increases in hip BMD of at least 0.019 g/cm², suggesting that there was a clinically significant response. However, the study also found large within-person variability in year-to-year bone density measurements. The average within-person variation in BMD measurement was 0.013 g/cm² relative to the placebo, which was substantially higher than the average annual increase in BMD in the alendronate group, 0.0085 g/cm². This finding suggests that the precision of BMD measurement is not reliable from year to year, and thus annual retesting may not be clinically useful. Additional studies would be needed to determine the optimal time interval for rescreening after starting bisphosphonate treatment.

Serial Measurement of Central BMD to Monitor Discontinuation of Bisphosphonate Treatment

In 2014, Bauer et al. reported on fracture risk prediction among women who discontinued alendronate after 4 to 5 years of treatment in the FLEX (Fracture Intervention Trial Long-term Extension) study. Women ages 61 to 86 years who had been treated with alendronate were randomized to 5 more years of alendronate or to placebo. A prior report of this study (2006) found that although hip BMD decreased in the placebo group, rates of fracture were similar between the group randomized to placebo and the group that continued on bisphosphonate therapy. It should be noted that alendronate has a half-life in humans that is estimated to exceed 10 years. During the 5 years of placebo treatment, 94 (22%) of 437 women experienced 1 or more symptomatic fractures; most (87%) occurred after 1 year. Post hoc analysis found that older age and lower hip (but not spine) DXA at time of discontinuation were significantly related to increased fracture risk; however, changes in BMD between the beginning of discontinuation to years 1 and 3 were not.

Summary of Evidence

For individuals who are eligible for screening of bone mineral density (BMD) based on risk factor assessment who receive dual x-ray absorptiometry (DXA) analysis of central sites (hip or spine), the evidence includes large cohort studies, observational studies, and systematic reviews. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, health status measures, quality of life, hospitalizations, medication use, and resource utilization. BMD measurements with central DXA identify individuals at increased risk of fracture. There is sufficient evidence that osteoporosis medications are effective at reducing
fracture risk in postmenopausal women with BMD in the osteoporotic range identified by central DXA. Therefore, a chain of evidence establishes that screening BMD with central DXA is likely to improve health outcomes. Evidence to support serial or repeat measurement of BMD is less compelling; nonetheless, the available evidence and the consensus of clinical evidence-based guidelines support at least a 2-year interval in BMD measurement to monitor response to pharmacologic therapy. Finally, available evidence suggests that at least a 3- to 5-year timeframe is reasonable for repeat measurement of BMD in individuals who initially tested normal and to monitor pharmacologic therapy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are eligible for screening of BMD based on risk factor assessment who receive ultrasound densitometry, or quantitative computed tomography, or DXA analysis of peripheral sites, the evidence includes observational studies and systematic reviews. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, health status measures, quality of life, hospitalizations, medication use, and resource utilization. These technologies are not commonly used for BMD measurements in practice and no studies have shown that they can select patients who benefit from treatment for osteoporosis. There is little to no evidence on the usefulness of repeat measurement of BMD using these techniques. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Supplemental Information**

**Clinical Input From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 4 physician specialty societies (7 reviewers) and 2 academic medical centers while this evidence review was under review in 2008. In addition, 7 unsolicited letters were received through 2 additional physician specialty societies. Reviewers agreed with the evidence review statement that an initial bone mineral density (BMD) test may be medically necessary. They also recommended an interval of 3 to 5 years between measurements in subjects who previously tested normal, depending on risk factors. Reviewers considered serial measurement of BMD important to guide treatment decisions (eg, continuing or changing medication).

Based on the consensus of clinical opinion on the value of the information provided by monitoring treatment response, serial BMD measurements (at least a 2-year interval) may be considered appropriate when this information will impact patient care. It should be noted that, with the margin of error of BMD measurements with
dual x-ray absorptiometry, questions remain about the interval over which a clinically significant change can be observed. The minimal clinically significant change also raises concerns about the potential for overinterpretation of small fluctuations with repeat testing.

**Practice Guidelines and Position Statements**

**American College of Obstetricians and Gynecologists**
In 2012 (reaffirmed 2014), the American College of Obstetricians and Gynecologists (ACOG) updated its guidelines on managing osteoporosis in women. The guidelines recommended that bone mineral density (BMD) screening should begin for all women at age 65 years. In addition, ACOG recommended screening for women younger than 65 years in whom the Fracture Risk Assessment (FRAX) Tool indicates a 10-year risk of osteoporotic fracture of at least 9.3%. Alternatively, ACOG recommended BMD screening for women in younger than 65 or with any of the following risk factors (they are similar, but not identical to risk factors in FRAX):

- Personal medical history of a fragility fracture
- Parental medical history of hip fracture
- Weight less than 127 lb
- Medical causes of bone loss (i.e., medications or disease)
- Current smoker
- Alcoholism
- Rheumatoid arthritis
- For women who begin medication treatment for osteoporosis, a repeat BMD is recommended 1 to 2 years later to assess effectiveness. If BMD is improved or stable, additional BMD testing (in the absence of new risk factors) is not recommended. The guideline notes that it generally takes 18 to 24 months to document a clinically meaningful change in BMD and thus a 2-year interval after treatment initiation is preferred to 1 year.
- The guidelines do not specifically discuss repeat BMD screening for women who have a normal finding on the initial test.
- Routine BMD screening is not recommended for newly menopausal women as a “baseline” screen.

**National Osteoporosis Foundation**
The National Osteoporosis Foundation (NOF) updated its practice guidelines in 2014. NOF guidelines recommended that all postmenopausal women and men ages 50 and older be evaluated clinically for osteoporosis risk to determine the need for BMD testing.

Indications for BMD testing included:

- “[W]omen age 65 and older and men age 70 and older” regardless of clinical risk factors
- “[P]ostmenopausal women and men above age 50-69, based on risk factors profile”
“[P]ostmenopausal women and men age 50 and older who have had an adult age fracture…”

“Adults with a condition ... or taking a medication ... associated with low bone mass or bone loss”

NOF stated that measurements for monitoring patients should be performed in accordance with medical necessity, expected response, and in consideration of local regulatory requirements. NOF recommended that repeat BMD assessments generally agree with Medicare guidelines of every 2 years, but recognized that testing more frequently may be warranted in certain clinical situations.

NOF also indicated that:

“Central DXA [dual x-ray absorptiometry] assessment of the hip or lumbar spine is the ‘gold standard’ for serial assessment of BMD. Biological changes in bone density are small compared to the inherent error in the test itself, and interpretation of serial bone density studies depends on appreciation of the smallest change in BMD that is beyond the range of error of the test. This least significant change (LSC) varies with the specific instrument used, patient population being assessed, measurement site, technologist’s skill with patient positioning and test analysis, and the confidence intervals used. Changes in the BMD of less than 3-6 % at the hip and 2-4 % at the spine from test to test may be due to the precision error of the testing itself.”

American College of Physicians

The 2008 guidelines from the American College of Physicians (ACP) recommended that clinicians periodically perform individualized assessment of risk factors for osteoporosis in men older than 50 years (grade: strong recommendation; moderate-quality evidence). Factors that increase the risk for osteoporosis in men included age (>70 years), low body mass index, weight loss, physical inactivity, corticosteroid use, androgen deprivation therapy, and previous fragility fracture. ACP recommended that clinicians obtain DXA for men who are at increased risk for osteoporosis and are candidates for drug therapy (grade: strong recommendation; moderate-quality evidence). The guidelines indicated that bone density measurement with DXA is the accepted reference standard for diagnosing osteoporosis in men; because treatment trials have not measured the effectiveness of therapy for osteoporosis diagnosed by ultrasound densitometry rather than DXA, the role of ultrasound in diagnosis remains uncertain. This evidence review found no studies that evaluated the optimal intervals for repeated screening by using BMD measurement with DXA in men.

American College of Radiology

Practice guidelines from the American College of Radiology, last amended in 2016, state that BMD measurement is indicated whenever a clinical decision is likely to be directly influenced by the result of the test. Indications for DXA included but were not limited to the following patient populations:
1. All women age 65 years and older and men age 70 years and older (asymptomatic screening)
2. Women younger than age 65 years who have additional risk for osteoporosis, based on medical history and other findings. Additional risk factors for osteoporosis include:
   a. Estrogen deficiency
   b. A history of maternal hip fracture that occurred after the age of 50 years
   c. Low body mass (less than 127 lb or 57.6 kg)
   d. History of amenorrhea (more than 1 year before age 42 years)
3. Women younger than age 65 years or men younger than age 70 years who have additional risk factors, including:
   a. Current use of cigarettes
   b. Loss of height, thoracic kyphosis
4. Individuals of any age with bone mass osteopenia, or fragility fractures on imaging studies such as radiographs, CT [computed tomography], or MRI [magnetic resonance imaging]
5. Individuals age 50 years and older who develop a wrist, hip, spine, or proximal humerus fracture with minimal or no trauma, excluding pathologic fractures
6. Individuals of any age who develop 1 or more insufficiency fractures
7. Individuals being considered for pharmacologic therapy for osteoporosis.
8. Individuals being monitored to:
   a. Assess the effectiveness of osteoporosis drug therapy.
   b. Follow-up medical conditions associated with abnormal BMD.

**International Society for Clinical Densitometry**

The 2013 update of the International Society for Clinical Densitometry guidelines recommended bone density testing in the following patients:

- “Women age 65 and older
- For post-menopausal women younger than age 65 a bone density test is indicated if they have a risk factor for low bone mass fracture such as;
  - Low body weight
  - Prior fracture
  - High risk medication use
  - Disease or condition associated with bone loss.
- Women during the menopausal transition with clinical risk factors for fracture, such as low bone weight, prior fracture or high-risk medication use.
- Men aged 70 and older.
- Men under < 70 years ... if they have a risk factors for low bone mass such as;
  - Low body weight
  - Prior fracture
  - High risk medication use
  - Disease or condition associated with bone loss.
- Adults with a fragility fracture.
- Adults with a disease or condition associated with low bone mass or bone loss....
- Anyone being considered for pharmacologic therapy.
- Anyone being treated, to monitor treatment effect.
Anyone not receiving therapy in whom evidence of bone loss would lead to treatment.”

American Association of Clinical Endocrinologists et al
In 2016, the American Association of Clinical Endocrinologists and American College of Endocrinology issued updated joint guidelines on the diagnosis and treatment of postmenopausal osteoporosis. The guidelines listed the potential uses for BMD measurements in postmenopausal women as:

- Screening for osteoporosis
- Establishing the severity of osteoporosis or bone loss...
- Determining fracture risk...
- Identifying candidates for pharmacologic intervention
- Assessing changes in bone density over time...
- Enhancing acceptance of, and perhaps adherence with, treatment
- Assessing skeletal consequences of diseases, conditions, or medications known to cause bone loss”

North American Menopause Society
The North American Menopause Society issued a 2010 position statement, which indicated that fracture is the most significant risk of low bone density. The statement also concluded that BMD is an important determinant of fracture risk, especially in women 65 years and older.

U.S. Preventive Services Task Force Recommendations
The U.S. Preventive Services Task Force (USPSTF) updated its recommendations on screening for osteoporosis with bone density measurements in January 2011. USPSTF recommended “screening for osteoporosis in women aged 65 years or older and in younger women whose risk of fracture is equal to or greater than that of a 65-year-old white woman who has no additional risk factors.” This represents a change from the previous (2002) version, in which there was no specific recommendation on screening in women younger than 65 years old. The supporting document notes that there are multiple instruments to predict risk for low BMD and that the USPSTF used FRAX. The updated USPSTF recommendations stated that the scientific evidence is “insufficient” to recommend for or against routine osteoporosis screening in men. The Task Force did not recommend specific screening tests but said that the most commonly used tests are DXA of the hip and lumbar spine and quantitative ultrasound of the calcaneus.

USPSTF recommended the following on BMD screening intervals: “A lack of evidence exists about the optimal intervals for repeat screening and whether repeated screening is necessary in a woman with normal BMD. Because of limitations in the precision of testing, a minimum of 2 years may be needed to reliably measure a change in BMD; however, longer intervals may be necessary to improve fracture risk prediction.”

USPSTF recommendations for osteoporosis screening are in the process of being updated as of February 2017.
Medicare National Coverage

The Centers for Medicare and Medicaid pays for a screening bone mass measurement (BMM) once every 2 years (at least 23 months have passed since the month the last covered BMM was performed). When medically necessary, Medicare may pay for more frequent BMMs. Examples include, but are not limited to, monitoring beneficiaries on long-term glucocorticoid (steroid) therapy of more than 3 months, and confirming baseline BMMs to permit monitoring of beneficiaries in the future.

Conditions for coverage of BMM can be found in chapter 15, section 80.5 of Pub. 100-02, Medicare Benefit Policy Manual. Medicare covers BMM under the following conditions:

1. “Is ordered by the physician or qualified nonphysician practitioner who is treating the beneficiary following an evaluation of the need for a BMM and determination of the appropriate BMM to be used....
2. Is performed under the appropriate level of physician supervision as defined in 42 CFR 410.32(b).
3. Is reasonable and necessary for diagnosing and treating the condition of a beneficiary who meets the conditions described in §80.5.6.
4. In the case of an individual being monitored to assess the response to or efficacy of an FDA-approved osteoporosis drug therapy, is performed with a dual-energy x-ray absorptiometry system (axial skeleton).
5. In the case of any individual who meets the conditions of 80.5.6 and who has a confirmatory BMM, is performed by a dual-energy x-ray absorptiometry system (axial skeleton) if the initial BMM was not performed by a dual-energy x-ray absorptiometry system (axial skeleton). A confirmatory baseline BMM is not covered if the initial BMM was performed by a dual-energy x-ray absorptiometry system (axial skeleton).”

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in February 2017 did not identify any ongoing or unpublished trials that would likely influence this review.

References


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**Billing Coding/Physician Documentation Information**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>76977</td>
<td>Ultrasound bone density measurement and interpretation, peripheral site(s)</td>
</tr>
<tr>
<td>77078</td>
<td>Quantitative Computerized Tomography bone mineral density study, one or more sites, axial skeleton (eg hips, pelvis spine)</td>
</tr>
<tr>
<td>77080</td>
<td>Dual energy x-ray absorptiometry (DEXA), bone density study, one or more sites; axial skeleton (eg, hips, pelvis, spine)</td>
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<tr>
<td>77081</td>
<td>Dual energy x-ray absorptiometry (DEXA), bone density study, one or more sites; appendicular skeleton (peripheral) (eg, radius, wrist, heel)</td>
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<tr>
<td>78350</td>
<td>Bone density (bone mineral content) study, 1 or more sites; single photon absorptiometry</td>
</tr>
<tr>
<td>78351</td>
<td>Bone density (bone mineral content) study, 1 or more sites; dual photon absorptiometry, 1 or more sites</td>
</tr>
<tr>
<td>G0130</td>
<td>Single energy x-ray absorptiometry bone density study, one or more sites; appendicular skeleton (peripheral - e.g., radius, wrist, heel)</td>
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</tbody>
</table>

**ICD10 Codes:**

- **M81.0** Age-related osteoporosis without current pathological fracture
- **M81.6** Localized osteoporosis
- **M81.8** Other osteoporosis without current pathological fracture
- **M85.80** Other specified disorders of bone density and structure, unspecified site

CPT codes 77079 and 77083 were deleted effective 1/1/2012.

**Additional Policy Key Words**

N/A

**Policy Implementation/Update Information**

10/1/88 New policy added to Radiology section. Considered medically necessary for high risk individuals and those receiving therapy for osteoporosis to monitor bone mass.
<table>
<thead>
<tr>
<th>Date</th>
<th>Changes</th>
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<tbody>
<tr>
<td>3/1/00</td>
<td>No policy statement change.</td>
</tr>
<tr>
<td>3/1/01</td>
<td>Additional high risk criteria added, definition updated to include description of various techniques that may be used.</td>
</tr>
<tr>
<td>3/1/02</td>
<td>Policy statement revised to indicate Appendicular studies are not medically necessary, low risk individuals are contract exclusions, and ultrasound of a peripheral site is investigational.</td>
</tr>
<tr>
<td>3/1/03</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>3/1/04</td>
<td>Policy statement revised to include current fracture or history of fracture in first-degree relative as a risk factor in the criteria for Postmenopausal women under age 65 who have one or more risk factors.</td>
</tr>
<tr>
<td>5/1/05</td>
<td>Policy statement revised to indicate <em>axial</em> bone mineral density by either DXA or QCT may be considered medically necessary for high risk individuals, added depo-provera to the list of high-risk, changed serial measurements from medically necessary to not medically necessary, changed ultrasound of any site to not medically necessary.</td>
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<tr>
<td>4/1/06</td>
<td>Clarified policy statement regarding patients who are at low risk for developing osteoporosis. Those individuals not meeting the criteria for high risk are considered low risk; bone density screening would therefore be a contract exclusion.</td>
</tr>
<tr>
<td>3/1/07</td>
<td>No policy statement changes. CPT codes updated, rationale updated.</td>
</tr>
<tr>
<td>3/1/08</td>
<td>Policy statement clarified to specify both women and men. Specific criteria are no longer in the policy statement. The description and rationale reference criteria used.</td>
</tr>
<tr>
<td>12/11/08</td>
<td>Interim update: Policy updated with literature review; references added and reordered. Clinical input reviewed. Policy statement added; repeat measurement (3-5 year interval) may be medically necessary if previously normal; serial testing (at least 2 year interval) changed to medically necessary. Policy title changed from Bone Density Studies to Bone Mineral Density Studies.</td>
</tr>
<tr>
<td>3/1/09</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>3/1/10</td>
<td>No policy statement changes. Policy clarified in Considerations section regarding reimbursement for peripheral scans.</td>
</tr>
<tr>
<td>3/1/11</td>
<td>No policy statement changes.</td>
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<td>5/1/16</td>
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<tr>
<td>3/1/17</td>
<td>No policy statement changes.</td>
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</table>
| 5/1/17   | The policy statements were edited to clarify that central dual x-ray absorptiometry (DXA) is medically necessary and other methods of measurement are investigational. A policy statement was added before the investigational statement that “Peripheral BMD testing could be considered medically necessary when conventional central (hip/spine) DXA screening is not feasible or in the management of hyperparathyroidism, where peripheral DXA measurement at the distal
forearm (ie, radius) is essential for evaluation.”

3/1/18 No policy statement changes.
6/1/18 Updated Considerations to include osteopenia. Added ICD10 M85.80.

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